

***Remarks***

Reconsideration of this application is respectfully requested. This Amendment amends the claims. Upon entry of this Amendment, claims 1-20, 23-25, 27-31, and 33-39 are pending in the application, with claim 1 being the independent claim. Claims 1, 2, 28-31, and 33 are amended. Claims 21, 22, 26, and 32 are canceled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested. Applicant asserts the right to file one or more continuing applications for the canceled subject matter. Support for the amendments can be found in the original specification and claims as filed. No new matter has been added by these amendments.

Claims 1 and 2 have been amended by deleting the possibility for X to be "NH", and revising the proviso to require that "when R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue, then R<sup>4</sup> is H." Support for the revised proviso can be found, *inter alia*, in original claims 28 and 29. Applicant submits that no new matter has been introduced by these amendments since deletion of individual members of Markush expression does not constitute new matter. See, *In re Johnson and Farnham*, 194 U.S.P.Q. 187 (CCPA 1977).

Claims 28-31 and 33 have been amended by adding "or a pharmaceutically acceptable salt thereof." at the end of each claim. Support for this amendment can be found in claim 1 as originally filed.

Based on the above amendment and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***I. Election Requirement***

Applicant notes that claims 4-7, 9, 11-13, 15, 18, 20, 22, 23, 25, 26, 28, 29, 32, and 33 are being withdrawn for allegedly being drawn to non-elected species, and claims 35-39 are being withdrawn for being drawn to non-elected group. According to the Examiner, claims 1-3, 8, 10, 14, 16, 17, 19, 21, 24, 27, 30, 31, and 34 read on the elected invention and are being examined.

The withdrawal of claims 4-7, 9, 11-13, 15, 18, 20, 22, 23, 25, 26, 28, 29, 32, and 33 is in error because the Examiner has treated the Election of Species Requirement as a Restriction Requirement. As stated in the Office Action at page 3, "[t]he species compound 75 was searched and found free of prior art (see claim objections below). The search was expanded by Examiner and two new species were found and which are herein both examined for the sake of compact prosecution." The elected species, compound 75, has  $R_1=H$  and  $R_2=CH_3$ . The Examiner expanded the search and all the rejections made in the Office Action are directed to compounds where  $R_1$  and  $R_2$  together form a proline residue and  $R_3$  is a naphthylmethyl group. However, claims directed to species where  $R_1$  and  $R_2$  do not form a proline ring have been withdrawn from consideration (claims 4 and 25).

M.P.E.P. § 803.02 states that:

[i]f on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration....

On the other hand, should \*\*>the examiner determine that< the elected species >is allowable<, the \*>examination< of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a *nonelected species*, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration.... Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended markush-type claim will be reexamined. The \*\*>examination< will be extended to the extent necessary to determine patentability of the Markush-type claim.

Accordingly, claims 4-7, 9, 11-13, 15, 18, 20, 22, 23, 25, 26, 28, 29, 32, and 33 should be considered on the merits.

Further, Applicant respectfully requests the Examiner rejoin the product claims with the method claims following a finding that the product claims are allowable, in accordance with M.P.E.P. § 821.04 and *In re Ochiai*, 37 U.S.P.Q. 1127 (Fed. Cir. 1995).

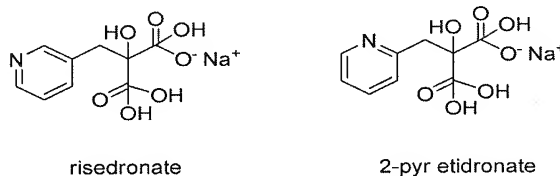
## ***II. Rejections Under 35 U.S.C. § 103***

### ***I. Legal Principles***

The courts have recently addressed the requirements for a determination of obviousness in the chemical compound area. *See KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727 (U.S. Sup. Ct. 2007); *Takeda v. Alphapharm*, 492 F.3d 1350 (Fed. Cir. 2007); *Takeda Chem. Indus. v. Mylan Labs.*, 549 F.3d 1381 (Fed. Cir. 2008); *Eisai Co., Ltd. v. Teva Pharms. USA, Inc.*, 533 F.3d 1353 (Fed. Cir. 2008). Under these recent decisions, the Office is required to (1) identify some reason that would have led a person of

ordinary skill in the art to select a particular compound as a "lead compound" in the cited reference; and (2) show that a reason existed, based on what was known at the time of the invention, to perform the chemical modifications necessary to achieve the presently claimed compounds. *See Takeda v. Alphapharm*, at 1362-1363.

This legal standard was reaffirmed with respect to the patentability of positional isomers in *The Procter & Gamble Company v. Teva Pharm. USA, Inc.*, 566 F.3d 989 (Fed. Cir. May, 2009) wherein the Federal Circuit held that 3-pyr etidronate (risedronate) was not obvious in view of prior art that disclosed 2-pyr etidronate. 566 F.3d at 995. The chemical structures of 3-pyr etidronate and 2-pyr etidronate are shown below:



## 2. *Schmidt et al.*

Claims 1 and 34 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schmidt *et al.* (*J. Peptide Res.*, 1999). Applicant respectfully traverses this rejection.

The Examiner states as follows at page 4, lines 11-14, of the Office Action:

Schmidt *et al.* disclose a compound encompassed by formula I. See, e.g. compound 47 in Table of page 149, notation to Figure 1, page 147, except that it does not teach the specific stereochemistry claimed.

Compound 47 of Schmidt *et al.* has X<sub>1</sub> as NH (corresponds to Applicant's X). Claim 1 has been amended by deleting the possibility for X to be NH. Furthermore, claim 1 has been amended by requiring that "when R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue, then R<sup>4</sup> is H."

Applicant submits that, in light of the case law relating to chemical compound patents, claim 1 as amended is not *prima facie* obvious over Schmidt *et al.* There is no reason in Schmidt *et al.* why a chemist would modify the compound No. 47, or any other compound purportedly described in Schmidt *et al.*, in a particular manner to arrive at compounds as claimed in amended claim 1 with a reasonable expectation of success. It follows that the compositions recited in claim 34, comprising the unobvious compounds of claim 1, are also unobvious.

In view of the above, Applicant respectfully requests that the rejection of claims 1 and 34 under 35 U.S.C. § 103(a) over Schmidt *et al.* be reconsidered and withdrawn.

**3.           Joullie *et al.* in view of Bren**

Claims 1, 2, 10, 14, 16, 17, 19, 21, 27, and 34 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Joullie *et al.* (WO 01/76616) in view of Bren (*J. Peptide Res.*, 1999). Applicant respectfully traverses this rejection as it applies to the claims as amended.

The Examiner argues as follows:

Joullie *et al.* teach didemnin and tamandarin analogs which have a deoxy-proline residue or a dehydro-proline residue in their structure. . . . Joullie *et al.* teach a compound of formula I wherein R<sub>3</sub> can be a fluorophore (e.g., pages 1-25, Figures 27-28, 32-40). Joullie *et al.* do not expressly

teach the fluorophore being "naphthylmethyl". Bren discloses organic fluorophores including, e.g., those containing naphthylmethyl as fluorophores (e.g., pages 1022 and 1027). It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace, e.g., the residue corresponding to R2 for a fluorophore . . . such as naphthylmethyl.

Office Action at page 5, line 20 through page 6, line 9.

Applicant has amended claim 1 by requiring that "when R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue, then R<sup>4</sup> is H." The compounds of Joullie *et al.* always have a methyl group in the position for R<sup>4</sup>.

Applicant submits that, in light of the case law relating to chemical compound patents, claim 1 as amended is not *prima facie* obvious over Joullie *et al.*, either alone or in combination with Bren. There is no reason in Joullie *et al.* why a chemist would modify, e.g., compound of Fig. 27, or any other compound purportedly described in Joullie *et al.*, in a particular manner to arrive at compounds as claimed in amended claim 1 with a reasonable expectation of success. Bren does not remedy the deficiencies of Joullie *et al.* In view of the above, Applicant also submits that the dependent claims 2, 10, 14, 16, 17, 19, 21, 27, and 34 are not *prima facie* obvious over Joullie *et al.*, either alone or in combination with Bren.

Applicant respectfully requests that this rejection under 35 U.S.C. § 103(a) over Joullie *et al.* in view of Bren be reconsidered and withdrawn. Claim 21 has been canceled.

**III. Objections**

Claims 3, 8, 24, 30, and 31 are objected to as allegedly being dependent upon a rejected base claim, but would be allowable is rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicant respectfully traverses this objection.

Applicant thanks the Examiner for indicating that claims 3, 8, 24, 30, and 31 include allowable subject matter.

In view of the above, claim 2 as amended is patentable over Joullie *et al.* in view of Bren and, thus, claims 3, 8, 24, 30, and 31 are dependent upon a patentable base claim. Applicant respectfully requests that the Examiner reconsider and remove the objection to claims 3, 8, 24, 30, and 31.

**III. Nonstatutory Obviousness-Type Double Patenting Rejections**

Claims 1, 2, 10, 14, 16, 17, 19, 21, 27, and 34 have been rejected on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-50 of U.S. Patent No. 6,509,315 ("US'315") in view of Bren; over claims 1-62 of U.S. Patent No. 7,064,105 ("US'105") in view of Bren; over claims 1-62 of U.S. Patent No. 7,122,159 [*sic*] ("US'519") in view of Bren; over claims 1-62 of U.S. Patent No. 7,651,997 ("US'997") in view of Bren; and over claims 1-62 of U.S. Patent No. 7,737,114 ("US'114") in view of Bren.

Applicant respectfully traverses all these rejections. Applicant assumes that U.S. Patent No. 7,122,159 cited by the Examiner should read U.S. Patent No. 7,122,519 that

was cited in a Supplemental Information Disclosure Statement filed on September 20, 2010.

According to M.P.E.P. § 804(II)(B)(1), "[a] nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claims because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s)." *See, e.g., In re Berg*, 140 F.3d 1428, 46 U.S.P.Q.2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 U.S.P.Q.2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 U.S.P.Q. 645 (Fed. Cir. 1985). Further, "[w]hen considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art." *See, General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 U.S.P.Q.2d 1839, 1846 (Fed. Cir. 1992).

The Examiner argues as follows:

Although the conflicting claims are not identical, they are patentably distinct from each other because they are both drawn to compounds of Formula I. Joullie et al. teach didemnin and tamandarin analogs which have a deoxo-proline residue or a dehydro-proline residue in their structure. . . . Joullie et al teach a compound of formula I wherein R3 can be a fluorophore (e.g., claims). Joullie et al. do not expressly teach the fluorophore being "naphthylmethyl". Bren discloses organic fluorophores including, e.g., those containing naphthylmethyl as fluorophores (e.g., pages 1022 and 1027). It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace, e.g., the residue corresponding to R2 for a fluorophore (see, e.g., claim 1) such as naphthylmethyl.



Office Action at page 8, lines 9-22.

Applicant respectfully disagrees. The claims of US'315, US'105, US'519, US'997, and US'114 all recite compounds having a proline residue (*i.e.*, R<sub>1</sub> and R<sub>2</sub> together form a ring of a proline residue in the present claims) and a methyl group at the position corresponding to R<sub>4</sub> of the present claims. As discussed above, Applicant has amended claims 1 and 2 by requiring that "when R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue, then R<sup>4</sup> is H". Accordingly, the claims as amended are not obvious over any of claims US'315, US'105, US'519, US'997, or US'114. Bren does not remedy the deficiencies of US'315, US'105, US'519, US'997, and US'114.

Therefore, reconsideration and withdrawal of this rejection under the judicially created doctrine of obviousness-type double patenting of claims 1, 2, 10, 14, 16, 17, 19, 21, 27, and 34 are respectfully requested. Claim 21 has been canceled.

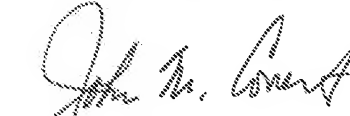
### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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